

**REMARKS/ARGUMENTS**

Claims 1, 4, 16-18, 20-26 and 28-30 are pending in this matter. Claims 23-26 and 28-30 have been allowed. Claims 1, 4, 16-18 and 20-22 remain rejected; however, in view of the remarks and Declaration included herein, Applicants submit that the remaining claims are also allowable. Reconsideration is respectfully requested.

**I. REJECTIONS UNDER 35 U.S.C. § 102(a)**

Claims 1, 4, and 16-20 stand rejected under 35 U.S.C. § 102(a) as allegedly being anticipated by Ahmad *et al.*, *Gastroenterology*, Vol. 122, pages 854-866 (Ahmad *et al.*, April 2002). In addition, claims 1, 4, and 16-20 were also rejected under 35 U.S.C. § 102(a) as allegedly being anticipated by Radlmayr *et al.*, *Gastroenterology*, Vol. 122, No. 7 pages 2091-2095 (June, 2002). In response, Applicants respectfully traverse the rejection.

The present application, U.S. Application No. 10/526,256 (“the ‘256 application”), is a national phase application arising from PCT Application No. PCT/03/023,926, (“PCT ‘926”) filed July 30, 2003. The PCT ‘926 application claims priority to U.S. Provisional Application No. 60/407,391, filed August 30, 2002 and U.S. Application No. 10/356,736, filed January 30, 2003.

As U.S. Provisional Application No. 60/407,391 was filed on August 30, 2002, Ahmad *et al.* (April 2002) and Radlmayr *et al.* (June 2002) are considered by the Examiner to be 35 U.S.C. § 102(a) art.

**A. Abreu *et al.***

Abreu *et al.*, *Gastroenterology*, Volume 123, Issue 3, pages 679-688 (2002) (“the Abreu *et al.* Vol. 123 reference, Sept 2002”) was published in September 2002 and embodies the claimed invention. The September 2002 date is verified by Exhibit 1, which is a copy of the “Table of Contents” from Volume 123, Issue 3 of the journal *Gastroenterology*. In order for the Abreu *et al.* Vol. 123 reference Sept 2002 to have been published in the September issue of 2002, it must have been received by the journal **before** September 2002.

In fact, it is clear from the Abreu *et al.*, Volume 123, reference on page 688, right hand column in the footnotes, that the manuscript (preprint) was received by the journal on **February 8, 2002**. February 8, 2002 **predates** both Ahmad *et al.* (April 2002) as well as Radlmayr *et al.* (June 2002).

The currently claimed rejected subject matter is embodied in the Abreu *et al.* Vol. 123 reference. The date of receipt of the manuscript by the journal *Gastroenterology* clearly antedates Ahmad *et al.* (April 2002) as well as Radlmayr *et al.* (June 2002).

**B. 37 CFR § 1.131 Declaration by the Inventors**

Applicants submit herewith a Declaration ("Declaration") under 37 CFR § 1.131, signed by each of the named inventors evidencing prior invention in the United States before the effective dates of each of the references. The Declaration has attached Exhibits A & B. Paragraphs 4-6 of the enclosed Declaration are reproduced below for the convenience of the Examiner and recite as follows:

4. Attached Exhibit A is a journal article that embodies the currently claimed invention. The journal article is entitled, "Mutations in NOD2 are associated with fibrostenosing disease in patients with Crohn's disease, by Maria T. Abreu, *et al.*, pages 679-688, Volume 123, Issue 3, (September 2002).

5. The Table of Contents of this September 2002 journal issue is attached as Exhibit B.

6. These Exhibits provide evidence of the conception of the invention and its reduction to practice. A manuscript, from which this journal article arose, was prepared prior to February 8, 2002. This is clear from the footnote on page 688 of the journal article, which states that the manuscript was received by the publisher on February 8, 2002.

Under MPEP § 715.07 it states:

The essential thing to be shown under 37 CFR 1.131 is priority of invention and this may be done by any satisfactory evidence of the

fact. FACTS, not conclusions, must be alleged. Evidence in the form of exhibits may accompany the affidavit or declaration. Each exhibit relied upon should be specifically referred to in the affidavit or declaration, in terms of what it is relied upon to show. [Emphasis added].

Applicants have provided the essential thing to show priority of invention. The date of the *declared* submission of the manuscript in the journal coupled with the date of publication of the article in the journal is satisfactory evidence of prior invention. Each of the inventors declares in paragraph 6:

...A manuscript, from which this journal article arose, was prepared prior to February 8, 2002.

Their declaration is corroborated by the journal itself by the footnote which recites: "Received February 8, 2002. Accepted March 16, 2002." In other words, according to the Declaration, a manuscript was prepared before February 8, 2002 and submitted to the journal for publication. The journal later published the manuscript in September 2002 and memorialized the date of receipt of the original manuscript as is customary and normal business practice. An actual copy of the manuscript is not required as the journal article itself is a facsimile of the accepted manuscript. The date of March 16, 2002 is the date of the actual acceptance of the manuscript by the journal, which date still predates the effective dates of either of the references.

**C. The Documentary Evidence Clearly Shows a Date *Prior* to the Effective Date of the References**

The Declaration and exhibits clearly state facts and evidence a date of invention in this country prior to the effective date of the cited references. When all the evidence is viewed in its entirety, including the Declaration, the Exhibits and later publication, Applicants' evidence clearly and convincingly establishes a date of invention prior to February 8, 2002. This date antedates the cited references.

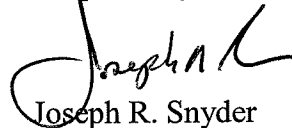
**D. A Timeline of Events**

Applicants have included a timeline of events as Exhibit 2 for the convenience of the Examiner. As shown therein, Applicants were clearly in possession of the invention prior to the publication of Ahmad *et al.* (April 2002) and Radlmayr *et al.* (June 2002).

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 925-472-5000.

Respectfully submitted,



Joseph R. Snyder  
Reg. No. 39,381

TOWNSEND and TOWNSEND and CREW LLP  
Two Embarcadero Center, Eighth Floor  
San Francisco, California 94111-3834  
Tel: 925-472-5000  
Fax: 415-576-0300  
Attachments  
JS:js  
62243113 v1

# **EXHIBIT 1**

View and discuss *Gastroenterology*  
video abstracts on YouTube™.



OFFICIAL JOURNAL OF  
THE AGA INSTITUTE

# Gastroenterology



OFFICIAL JOURNAL OF  
THE AGA INSTITUTE

Register or Login:  Password:  ☐ Auto-Login (Reminder)

Search This Periodical  for

Advanced Search - MEDLINE - My Recent Searches - My Saved Searches - Search Tips

## JOURNAL HOME

### CURRENT ISSUE

### PREVIOUS ISSUES

### ARTICLES IN PRESS

### POPULAR CONTENT

#### • Top 10 Most Read

#### Articles

#### • Top Cited Articles

### ARTICLE COLLECTIONS

- Video Abstracts
- Gastroenterology and Hepatology News
- Comments from the Editors

- Clinical Challenges and Images in GI
- Imaging and Advanced Technology

- Reviews in Basic and Clinical Gastroenterology
- AGA Institute Position Papers

- Selected Summaries
- Print and Media Reviews

- Mini-Reviews and Perspectives
- Correspondence
- Plenary Papers
- Meeting Summaries

### INFO FOR AUTHORS

- Submit a Manuscript
- Instructions for Authors
- Figure FAQs
- Medical Illustration

### FAQs

- Abstracting/Indexing
- Copyright Form
- CONSORT Checklist
- Style Guide
- Permission to Reuse

### ONLINE CME

### SUBSCRIBE

### FREE ISSUE

### JOIN AGA

### SHARED SCIENCE

### JOURNAL INFORMATION

- About Gastroenterology
- Contact Information
- Board of Editors
- Editorial Board
- Editorial Staff
- Info for Advertisers
- Press Embargo

### ACTIVATE ONLINE ACCESS

### SIGN UP FOR E-ALERTS



## GI LEARN

www.gilearn.org

## Issue

Alert me when new journal issues are available via

◀ previous issue    next issue ▶

## Gastroenterology

Volume 123, Issue 3, Pages 661-958 (September 2002)

display checked docs export citations e-mail articles

Display:  without preview

**FREE** = free full text

**This month in Gastroenterology** **FREE**

Joseph H. Sellin

pages 661-662

Abstract | [Full Text](#) | [Full-Text PDF \(75 KB\)](#)

### Gastroenterology News

**AGA a key to HELP committee passage of colorectal cancer screening expansion**

Leslie Lang

page 663

Abstract | [Full Text](#) | [Full-Text PDF \(51 KB\)](#)

**NIH set to expand digestive diseases study section**

Leslie Lang

page 663

Abstract | [Full Text](#) | [Full-Text PDF \(51 KB\)](#)

**AGA research policy initiatives**

Leslie Lang

page 664

Abstract | [Full Text](#) | [Full-Text PDF \(51 KB\)](#)

**Increased need for PhDs in gastrointestinal research**

Leslie Lang

page 664

Abstract | [Full Text](#) | [Full-Text PDF \(51 KB\)](#)

### Comment from the Editors

**The real meaning of translational research** **FREE**

Lloyd Mayer

page 665

Abstract | [Full Text](#) | [Full-Text PDF \(38 KB\)](#)

**Image of the month** **FREE**

Nahum Méndez-Sánchez, Maria Teresa Reyes, Roberto Corona, Misael Uribe

page 666

Abstract | [Full Text](#) | [Full-Text PDF \(95 KB\)](#)

### Clinical-Alimentary Tract

**Paradoxical coexpression of proinflammatory and down-regulatory cytokines in intestinal T cells in childhood celiac disease**

Göte Forsberg\*,†, Olle Hemell†, Silvia Melgar\*, Anne Israelsson\*, Sten Hammarström\*, Marie-Louise Hammarström\*

pages 667-678

Abstract | [Full Text](#) | [Full-Text PDF \(306 KB\)](#)

**Mutations in NOD2 are associated with fibrostenosing disease in patients with Crohn's disease**

Maria T. Abreu, Kent D. Taylor, Ying-Chao Lin, Tieu Hang, Joanne Gaennie, Carol J. Landers, Eric A. Vasilias, Lori Y. Kam, Micha Rojany, Konstantinos A. Papadakis, Jerome I. Rotter, Stephan R. Targan, Huiying Yang

pages 679-688

Abstract | [Full Text](#) | [Full-Text PDF \(141 KB\)](#)

**Selected loss of tolerance evidenced by Crohn's disease-associated immune responses to auto- and microbial antigens**

Carol J. Landers, Offer Cohavy, Rajeev Misra, Huiying Yang, Ying-Chao Lin, Jonathan Braun, Stephan R. Targan

pages 689-699

Abstract | [Full Text](#) | [Full-Text PDF \(310 KB\)](#)

### Biographical Sketch

**Meigs of Meigs' Syndrome** **FREE**

William S. Haubrich

page 699

Abstract | [Full Text](#) | [Full-Text PDF \(53 KB\)](#)

### Clinical-Alimentary Tract



## More periodicals:

[FIND A PERIODICAL](#)
[FIND A PORTAL](#)
[GO TO PRODUCT CATALOG](#)

#### Lipid-induced intestinal gas retention in irritable bowel syndrome

Jordi Serra, Beatrice Salvioli, Fernando Azpiroz, Juan-R. Malagelada

pages 700-706

[Abstract](#) | [Full Text](#) | [Full-Text PDF \(108 KB\)](#)

#### Predictors of response to infliximab in patients with Crohn's disease

Mansour A. Parsi, Jean-Paul Achkar, Scott Richardson, Jeffry Katz, Jeffrey P. Hammel, Bret A. Lashner, Aaron Brzezinski

pages 707-713

[Abstract](#) | [Full Text](#) | [Full-Text PDF \(92 KB\)](#)

#### Uveitis and erythema nodosum in inflammatory bowel disease: Clinical features and the role of HLA genes

Timothy R. Orchard, C.N. Chua, Tariq Ahmad, Hung Cheng, Kenneth I. Welsh, Derek P. Jewell

pages 714-718

[Abstract](#) | [Full Text](#) | [Full-Text PDF \(97 KB\)](#)

### **Clinical-Liver, Pancreas, and Biliary Tract**

#### Determinants of early mortality in patients with decompensated chronic hepatitis B treated with antiviral therapy

Robert J. Fontana, Hie-Won L. Hann, Robert P. Perrillo, John M. Vierling, Theresa Wright, Jorge Rakela, Gaya Anshuetz, Randy Davis,

Stephen D. Gardner, Nathaniel A. Brown

pages 719-727

[Abstract](#) | [Full Text](#) | [Full-Text PDF \(106 KB\)](#)

#### Banding ligation versus nadolol and isosorbide mononitrate for the prevention of esophageal variceal rebleeding

Gin-Ho Lo, Wen-Chi Chen, Mei-Hsiu Chen, Ping-I Hsu, Chiun-Ku Lin, Wei-Lun Tsai, Kwok-Hung Lai

pages 728-734

[Abstract](#) | [Full Text](#) | [Full-Text PDF \(116 KB\)](#)

#### Primary prophylaxis of variceal hemorrhage: A randomized controlled trial comparing band ligation, propranolol, and isosorbide mononitrate

Hock F. Lui, Adrian J. Stanley, Ewan H. Forrest, Rajiv Jalan, W. Stuart Hislop, Peter R. Mills, Niall D.C. Finlayson, Alastair J. Macgillchrist,

Peter C. Hayes

pages 735-744

[Abstract](#) | [Full Text](#) | [Full-Text PDF \(104 KB\)](#)

#### The utility of radiological imaging in nonalcoholic fatty liver disease

Sherif Saadeh\*, Zobair M. Younossi\*,†, Erick M. Remer\$, Terry Gramlich□, Janus P. Ong†, Maja Hurley\$, Kevin D. Mullen\*, James N.

Cooper†, Michael J. Sheridan†

pages 745-750

[Abstract](#) | [Full Text](#) | [Full-Text PDF \(80 KB\)](#)

### **Basic-Alimentary Tract**

#### The APC tumor suppressor controls entry into S-phase through its ability to regulate the cyclin D/RB pathway

Christopher D. Heinen, Kathleen Heppner Goss, James R. Comelius, George F. Babcock, Erik S. Knudsen, Timothy Kowalik, Joanna

Grodén

pages 751-763

[Abstract](#) | [Full Text](#) | [Full-Text PDF \(407 KB\)](#)

#### JunD stabilization results in inhibition of normal intestinal epithelial cell growth through P21 after polyamine depletion

Li Li\*,†, Lan Liu\*,†, Jaladanki N. Rao\*,†, Ali Esmaili\*, Eric D. Strauch\*, Barbara L. Bass\*,†, Jian-ying Wang\*,†,§

pages 764-779

[Abstract](#) | [Full Text](#) | [Full-Text PDF \(1023 KB\)](#)

#### Fas/CD95 is required for gastric mucosal damage in autoimmune gastritis

Aiden C.J. Marshall, Frank Alderuccio, Ban-Hock Toh

pages 780-789

[Abstract](#) | [Full Text](#) | [Full-Text PDF \(592 KB\)](#)

#### HMGB1 B box increases the permeability of Caco-2 enterocytic monolayers and impairs intestinal barrier function in mice

Penny L. Sappington\*, Runkuan Yang\*, Huan Yang†, Kevin J. Tracey†, Russell L. Delude\*,§, Mitchell P. Fink\*,□

pages 790-802

[Abstract](#) | [Full Text](#) | [Full-Text PDF \(278 KB\)](#)

#### Celiac lesion T cells recognize epitopes that cluster in regions of gliadins rich in proline residues

Helene Arentz-Hansen, Stephen N. Mcadam, Øyvind Molberg, Burkhard Fleckenstein, Knut E.A. Lundin, Thomas J.D. Jørgensen,

Günther Jung, Peter Roepstorff, Ludvig M. Sollid

pages 803-809

[Abstract](#) | [Full Text](#) | [Full-Text PDF \(130 KB\)](#)

#### The type of sodium-coupled solute modulates small bowel mucosal injury, transport function, and ATP after ischemia/reperfusion injury in rats

Rosemary A. Kozar\*, Stanley G. Schultz†, Heitham T. Hassoun\*, Roland Desoigne\*, Norman W. Weisbrodt†, Marian M. Haber□,

Frederick A. Moore\*

pages 810-816

[Abstract](#) | [Full Text](#) | [Full-Text PDF \(333 KB\)](#)

#### Expression of human intestinal mucin is modulated by the β-galactoside binding protein galectin-3 in colon cancer

Steven P. Dudas, Christopher K. Yunker, Lawrence R. Sternberg, James C. Byrd, Robert S. Bresalier

pages 817-826

[Abstract](#) | [Full Text](#) | [Full-Text PDF \(1594 KB\)](#)

#### Coupling of M<sub>2</sub> muscarinic receptor to L-type Ca<sup>2+</sup> channel via c-src kinase in rabbit colonic circular smooth muscle

Xiaochun Jin, Nemat Morsy, Fouzia Shoeb, Joelle Zavzavadjian, Hamid I. Akbarali

pages 827-834


[Abstract](#) | [Full Text](#) | [Full-Text PDF \(172 KB\)](#)

### **Basic-Liver, Pancreas, and Biliary Tract**

#### Hepcidin expression inversely correlates with the expression of duodenal iron transporters and iron absorption in rats

David M. Frazer, Sarah J. Wilkins, Erika M. Becker, Christopher D. Vulpe, Andrew T. Mckie, Deborah Trinder, Gregory J. Anderson

pages 835-844


 [Abstract](#) | [Full Text](#) | [Full-Text PDF \(1016 KB\)](#)

---

**Caspase 9-dependent killing of hepatic stellate cells by activated Kupffer cells**

Richard Fischer, Alexandra Cariers, Roland Reinehr, Dieter Häussinger

pages 845-861

 [Abstract](#) | [Full Text](#) | [Full-Text PDF \(738 KB\)](#)


---

**Special Reports and Reviews**

**Emerging concepts in colorectal neoplasia**

Jeremy R. Jass, Vicki L.J. Whitehall, Joanne Young, Barbara A. Leggett

pages 862-876

 [Abstract](#) | [Full Text](#) | [Full-Text PDF \(306 KB\)](#)


---

**American Gastroenterological Association**

**Joint statement on missions and submissions of papers to AGA journals** **FREE**

David A. Brenner, Michael Camilleri


pages 877-878

 [Abstract](#) | [Full Text](#) | [Full-Text PDF \(39 KB\)](#)

---

**American Gastroenterological Association medical position statement on Obesity. This document presents the official recommendations of the American Gastroenterological Association (AGA) on Obesity. It was approved by the Clinical Practice Committee on March 3, 2002 and by the AGA Governing Board on May 19, 2002.** **FREE**

pages 879-881

 [Abstract](#) | [Full Text](#) | [Full-Text PDF \(52 KB\)](#)


---

**American Gastroenterological Association**

**AGA technical review on obesity** **FREE**

Samuel Klein, Thomas Wadden, Harvey J. Sugerman

pages 882-932

 [Abstract](#) | [Full Text](#) | [Full-Text PDF \(523 KB\)](#)


---

**Editorials**

**Much to do about gas** **FREE**

Michael Camilleri, Silvia Delgado-Aros

pages 933-935


 [Abstract](#) | [Full Text](#) | [Full-Text PDF \(67 KB\)](#)

---

**APC as a checkpoint gene: The beginning or the end?** **FREE**

Vincent W. Yang

pages 935-939

 [Abstract](#) | [Full Text](#) | [Full-Text PDF \(151 KB\)](#)

---

**Celiac disease pathogenesis: The plot thickens** **FREE**

Martin F. Kagnoff

pages 939-943

 [Abstract](#) | [Full Text](#) | [Full-Text PDF \(77 KB\)](#)


---

**Selected Summaries**

**And now...fattening the lower esophageal sphincter** **FREE**

Sreenivasa Jonnalagadda

pages 944-946

 [Abstract](#) | [Full Text](#) | [Full-Text PDF \(88 KB\)](#)

---

**More than food trafficks into the esophagus** **FREE**

Glenn T. Furuta

pages 946-947


 [Abstract](#) | [Full Text](#) | [Full-Text PDF \(90 KB\)](#)

---

**Viral discrimination and subversion of host defense at the epithelial gateway** **FREE**

Fergus Shanahan

pages 947-948


 [Abstract](#) | [Full Text](#) | [Full-Text PDF \(90 KB\)](#)

---

**In search of vulcan: Where are all the iron men (and women)?** **FREE**

George N. Ioannou, Kris V. Kowdley

pages 948-950

 [Abstract](#) | [Full Text](#) | [Full-Text PDF \(90 KB\)](#)


---

**Print and Media Reviews**

**Shackelford's Surgery of the Alimentary Tract, 5th Edition** **FREE**

Mark J. Koruda

pages 951-952


 [Abstract](#) | [Full Text](#) | [Full-Text PDF \(52 KB\)](#)

---

**Positive Options for Living with Your Ostomy: Self-Help and Treatment** **FREE**

Ann Woodruff

pages 952-953


 [Abstract](#) | [Full Text](#) | [Full-Text PDF \(52 KB\)](#)

---

**The First Year—Crohn's Disease and Ulcerative Colitis: An Essential Guide for the Newly Diagnosed** **FREE**

Anthea L. Darling

page 953

 [Abstract](#) | [Full Text](#) | [Full-Text PDF \(52 KB\)](#)

---


**Correspondence**



**Reply**


Ulrich Wahnschaffe

page 954

 [Abstract](#) | [Full Text](#) | [Full-Text PDF \(77 KB\)](#)**Gastric surgery and Barrett's esophagus** **FREE**


Pascual Parrilla

page 954

 [Abstract](#) | [Full Text](#) | [Full-Text PDF \(77 KB\)](#)**Celiac disease-like abnormalities in IBS: Wrong title or wrong disease?** **FREE**


Pierre Poitras

page 954

 [Abstract](#) | [Full Text](#) | [Full-Text PDF \(77 KB\)](#)**Mucosal flora in inflammatory bowel disease: Intraepithelial bacteria or endocrine epithelial cell secretory granules?**


Jerry S. Trier

page 955

 [Abstract](#) | [Full Text](#) | [Full-Text PDF \(77 KB\)](#)**Discussion on preoperative prevalence of Barrett's esophagus in esophageal adenocarcinoma: A systemic review** **FREE**


Martin Gough, Clive Kelly, Nigel Bird, Ali Majeed, Roger Ackroyd

page 955

 [Abstract](#) | [Full Text](#) | [Full-Text PDF \(77 KB\)](#)**Reply** **FREE**


Gareth S. Dulai, Sushovan Guha, Katherine L. Kahn, Jeffrey Gornbein, Wilfred M. Weinstein

page 955

 [Abstract](#) | [Full Text](#) | [Full-Text PDF \(77 KB\)](#)**"High-grade MALT" vs. diffuse large B cell lymphoma**


Scott A. Cely

page 956


 [Abstract](#) | [Full Text](#) | [Full-Text PDF \(77 KB\)](#)**Reply**

Alexander Swidsinski

page 956

 [Abstract](#) | [Full Text](#) | [Full-Text PDF \(77 KB\)](#)**Image of the Month****Answer to the image of the month question (page 666) Pyogenic liver abscess complicated by bronchial fistula**


page 957

 [Abstract](#) | [Full Text](#) | [Full-Text PDF \(51 KB\)](#)**Correspondence****Correction**


page 957

 [Abstract](#) | [Full Text](#) | [Full-Text PDF \(51 KB\)](#)**Notices**


page 958

 [Preview](#) | [Full Text](#) | [Full-Text PDF \(53 KB\)](#)**Frontmatter****Editorial Board**


page A1

 [Preview](#) | [Full Text](#) | [Full-Text PDF \(35 KB\)](#)**Copyright Assignment, Authorship Responsibility, Financial Disclosure, and Institutional Review Board/Animal Care Committee Approval**


page A1

 [Preview](#) | [Full Text](#) | [Full-Text PDF \(28 KB\)](#)**Style Guide**






page A1

 [Preview](#) | [Full Text](#) | [Full-Text PDF \(66 KB\)](#)**Forthcoming articles**

page A1

 [Preview](#) | [Full Text](#) | [Full-Text PDF \(33 KB\)](#)**Image of the Month Instruction for Authors**

page A1

 [Preview](#) | [Full Text](#) [display checked docs](#)  [export citations](#)  [e-mail articles](#)Display: [without preview](#) 

The content on this site is intended for health professionals.

# **EXHIBIT 2**

## Timeline of Events

